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Separating the Effects of Lead and Social Factors on IQ[1]

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Initial evaluations of 104 low-socioeconomic status black children screened by the local community health departments in North Carolina showed significant effects of lead in the range 6–59 μg/dl on IQ after controlling for concomitant social factors, such as socioeconomic status, home environment, and maternal IQ. The main concomitant variable was socioeconomic status, which was multicolinear with other social factors. Five years later, when all blood lead levels were 30 μg/dl or less, lead effects on IQ were no longer significant. The correlation between maternal and child IQ, which had been suppressed initially in children with higher lead levels, returned to expected levels when decreases in blood lead level occurred, while concomitant variables remained stable over the 5-year period. © 1985 Academic Press, Inc.

Children with incompletely developed nervous systems are considered a special risk group for the neurobehavioral effects of lead. Extreme levels (blood lead level 100 μg/dl) are associated with lead encephalopathy, which begins with dullness, restlessness, irritability, headaches, and muscular tremor and proceeds to convulsions, paralysis, coma, and frequently death. Even when chelation therapy is appropriately and quickly employed, death still occurs in 20–40% of encephalopathy cases (Ennis and Harrison, 1950; Agerty, 1952; National Academy of Sciences, 1972). In fact, chelation therapy may even hasten death when the severity of symptoms and blood lead level are underestimated. High lead levels that remain asymptomatic in terms of acute encephalopathy have been clearly associated with intellectual deficits which are frequently long lasting (Byers and Lord, 1943; Chisolm, 1968; Perlstein and Attala, 1966). Given that blood lead levels in the range 80 μg/dl and greater are generally proven to be extremely harmful, the question arises as to what effect lower levels such as 30–80 μg/dl may have. Answers to this question are inconsistent and contradictory. Many studies have shown that moderate lead exposure has significant effects on neurobehavioral (including cognitive) functioning (EPA, in press). Other studies report no such relation.

Tremendous controversy surrounds these studies regarding selection bias, sensitivity of instruments, indices of exposure, control of confounding covariates.

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blind evaluation, and appropriate statistics. As one might expect, this research is difficult to do from the standpoint of sample selection and experimentally rigorous control. Many studies fail to take into account such factors as socioeconomic status (SES), maternal intelligence, and quality of the caregiving environment. Others have examined older children several years after lead exposure, increasing the probability that intervening events have either exacerbated or minimized the effects of lead exposure. Many studies fail on a crucial statistical control procedure, i.e., to test interaction effects of lead and various control variables upon the various dependent measures. For example, consider the interaction of parental SES, lead, and IQ. Most studies have statistically "controlled" SES and tested the lead effect on IQ. Suppose, in actuality, that the relationship of lead to IQ differs as a function of SES. This is not an unreasonable question, since SES has been shown to interact with other environmental insults such as low birth weight. Such an effect would be missed if appropriate interactions were not tested.

Relative to the first point, analysis of covariance is probably not appropriate for these studies because it is likely that regression coefficients are not equal across groups. The various interaction vectors provide a powerful test for homogeneity of regression.

Another general criticism deals with a common failure to assess possible *dissociative aspects* of lead intoxication. Such an assessment is easily accomplished by intercorrelating all control and dependent measures separately in the several lead groups; e.g., consider parental SES, parental IQ, and child IQ. Suppose that in the low lead group parental SES and parental IQ are highly related to proband IQ. These relationships should be somewhat weaker in the high lead group. If this does not occur, it would lead one to suspect either (a) parent–child covariance on lead intoxication, (b) mean difference (on IQ) as a function of lead due to confounding with the various familiar variables, or (c) both possibilities.

Restriction of subjects to high-risk groups, such as blacks, severely restricts generalizability of a study. Consider the relation between child IQ and parental SES in blacks and whites. For example, the relationship between child IQ and parental SES is much stronger among whites than among blacks. Therefore, IQ may be less correlated with lead intoxication in blacks than in whites. If both variables are included, an interaction vector will test for the above possibility.

Order of entry of predictor variables in a regression analysis may be crucial in determining the result with nonorthogonal predictors. For example, consider three interrelated variables: early central nervous system (CNS dysfunction, age, and handedness. When age (at time of testing) is partialed out of handedness, CNS dysfunction continues to predict left-handedness. However, when CNS dysfunction is partialed out of handedness, age at time of testing has zero relationship to handedness.

Thus, obtaining an age effect depends on the ordering of variables in the equation. This ordering should always be guided by theory, so as not to capitalize on chance, but different orderings on the same data are generally useful when attempting causal modeling.

INITIAL SCREENING STUDY

Our initial research project was designed to investigate possible subtle cognitive deficits resulting from undue lead exposure and the relationship between lead and hyperactivity. The present study is concerned with the relationship among various factors and IQ. Specifically, the covariates considered important in children include parental socioeconomic status (Needleman *et al.*, 1979), maternal IQ (Perino and Ernhart, 1974), pica (Barltrop, 1966), home environment (Milar *et al.*, 1981), and age at exposure. These covariates are believed to be particularly important when considering "threshold effects" of lead. Thus, covariates may interact to pose a cumulative risk which may have differential weight given different lead levels (EPA, in press). This study represents only one small aspect of a larger research project and of the comprehensive evaluation which the children received, but it is one of the main topics of current research controversy.

Method

Subjects. One hundred and four children in Wake County, North Carolina, aged 10 months to 6½ years at the time of initial testings, served as subjects. They were mostly black (94%) from lower social classes, i.e., $\bar{x} = 4.5$ on the Hollingshead Two-Factor Index (Hollingshead and Redlich, 1958). Children previously evidencing CNS disease or insult and children with prediagnosed language delay or mental retardation were excluded from data analysis. Approximately half of the children were less than 30 months of age and half were over 30 months of age. Half of the subjects were EPSDT children and half were children of battery factory workers referred from a local county health department to the lead screening program at North Carolina Memorial Hospital as part of a statewide screening program.

Procedure. The order of evaluation was the same for all children. At the time of testing, the examiner was blind as to the child's lead exposure. The first evaluation consisted of an intellectual assessment using the Bayley Scales of Infant Development, mental development index (Bayley, 1969) for children less than 30 months of age and the Stanford-Binet Intelligence Scale (Terman and Merrill, 1960) for children 30 months of age or older. The second evaluation was a measure of free field activity (Routh *et al.*, 1974). We have reported these results elsewhere (Milar *et al.*, 1981) and will not discuss hyperactivity here.

While the child's intellectual evaluation was taking place, the primary caregiver (in most cases the mother) was interviewed by the patient coordinator. The following areas were covered: (1) family composition; (2) previous and present residence of child; (3) symptoms relating to lead poisoning; (4) socioeconomic background of parents including education and employment (Hollingshead and Redlich, 1958); (5) Werry–Weiss–Peters Activity Scale (Werry, 1968); (6) Conner's rating scale (Conners, 1969); (7) estimate of parental intelligence using the Ammons and Ammons Quick Test (1962).

Each child was also seen by a pediatrician for a complete medical evaluation. The purpose of this evaluation was to screen for medical problems not related to

lead that could contribute to delayed development. The last event of the day was a venous blood sample for lead level and other biochemical determinations.

Following the evaluation, a home visit was made to the primary residence of each child. During the visit, the mother was interviewed and the Home Observation for Measurement of the Environment (HOME) inventory developed by Caldwell was completed. This inventory is an overall indicator of the quality of the caregiving environment. Bradley and Caldwell (1976) have demonstrated a significant relationship between HOME score, intellectual performance, and language delay (Wulbert *et al.*, 1975). In particular, the subscales dealing with the emotional and verbal responsivity of the mother and the maternal involvement with the child showed the highest relationship.

Two different forms of the HOME inventory were used depending on the age of the child. For children under 30 months of age, the 45-item scale designed for younger children was used. For children over 30 months of age, the 80-item HOME inventory designed for children 3 to 6 years of age was used. All data were collected at a time when both mother and child were present. At the time of assessment the interviewer was blind as to the possible lead exposure of the children.

During the home visit, X-ray fluorimeter readings were taken on painted surfaces to evaluate possible lead hazard from paint. Dust samples were also obtained from the floor to evaluate the possible contribution of lead in the house dust to lead hazard. Results have been reported elsewhere (Milar and Mushak, 1982).

Results

The analytical plan involved exploratory analysis of the data as part of a larger project in which several other hypotheses were also tested (Otto *et al.*, 1985). The plan employed a form of hierarchical regression accomplished with backward stepwise regression (Kleinbaum *et al.*, 1982). The initial full model included the following sets of predictors: (1) linear, quadratic, and cubic components of lead; (2) concomitant variables comprised of the Caldwell HOME score, maternal IQ, the child's chronological age and sex, socioeconomic status of parents, test (Bayley vs Stanford-Binet), presence of the father in the home, and number of siblings; and (3) the omnibus interaction term between the first three components of lead (linear, quadratic, and cubic) and all concomitant variables. Only linear components of the concomitant variables were used because many studies have reported the lack of curvilinear relationships with IQ (e.g., Willerman, 1979).

The three sources were backstepped out of the full model in reverse order, i.e., (3) first and (1) last. A significant lead × concomitant variable interaction would lead to decomposition of the omnibus component.

The source summary is presented in Table 1. Only the socioeconomic status and the linear component of lead are significant. The concomitant variables had been removed from the equation simultaneously, and the only concomitant variable to reach statistical significance is socioeconomic status: regression coefficient = 0.375, $F(1,63) = 7.496$, $P < 0.01$. The regression coefficient for lead is

TABLE 1
SOURCE TABLE OF THE EFFECTS OF LEAD ON CHILDREN'S IQ (1977–1978 INITIAL STUDY)

Source	*df*	*ss*	*F*	*P*
Lead (linear)	1	1530.549	7.689	<0.01
Socioeconomic status	1	4012.906	20.159	<0.001
Residual	96	199.055		

−0.199. The failure of the omnibus interaction term to reach significance obviated the necessity for analyzing this source any further. The zero-order (linear) relationships between IQ and lead and IQ and socioeconomic status are presented in Fig. 1 and 2, respectively.

The failure of concomitant variables other than socioeconomic status to reach significance is probably due to multicolinearity. The multiple correlation (R) of this variable with all other concomitant variables = 0.677. The intercorrelation matrix of concomitant variables, lead, and IQ is presented in Table 2.

5-YEAR FOLLOW-UP STUDY

Approximately 5½ years later we retested these children to see whether there were any residual effects of early exposure that might show up at school age. Because all the children had grown out of the high-risk toddler stage, we expected all blood lead levels to be low.

Method

Subjects. Of the 104 children originally seen in 1977–1978, 80 were located through the county health department and school records. Each family received a letter inviting them to participate in the study and a telephone call from the

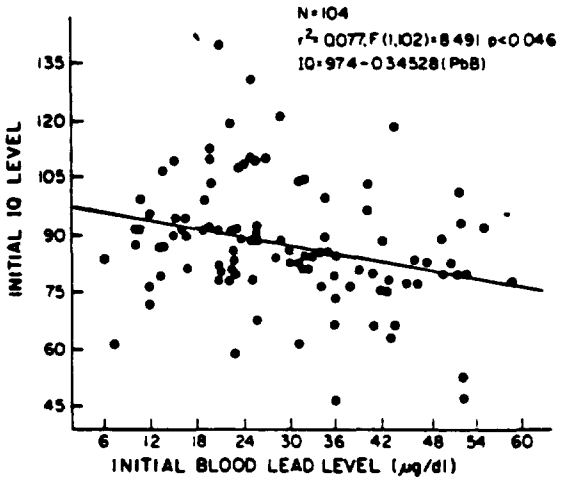

FIG. 1. Initial IQ levels as a function of initial blood lead levels (data collected 1977–1978).

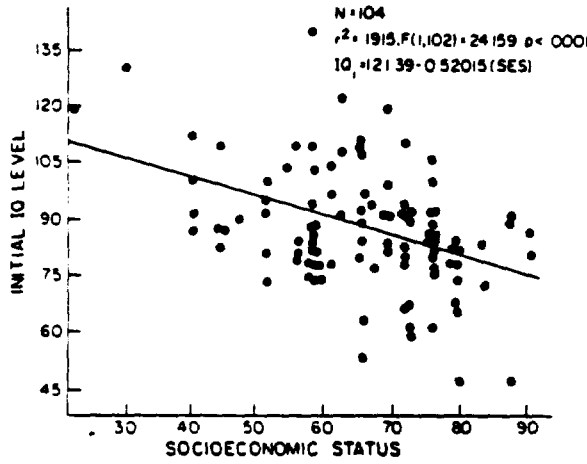

FIG. 2. Initial IQ levels as a function of initial socioeconomic status (1977–1978) using the Hollingshead Two-Factor Index.

nurse coordinator of the lead screening clinic explaining the study. The parents of 50 children agreed to participate.

Procedures. Children were seen at the local county health department in a mobile laboratory where they received a physical examination, an extensive family history using the Fantus Clinic Lead Poisoning Questionnaire, and a Stanford-Binet IQ test. Socioeconomic status (Hollingshead Two-Factor Index) and maternal IQ (Ammons and Ammons Quick Test) were repeated, but a home visit and the Caldwell HOME inventory were not. Electrophysiological tests were also made and are treated in a separate paper (Otto *et al.*, 1985).

Results and Discussion

Figure 7 shows that all of the children's blood lead levels 5 years later were equal to or below 30 μg/dl. A regression model similar to that used in the initial study was used for these data, except that "test" was no longer a variable since all children took the Stanford-Binet IQ test this time. "Age" was also dropped due to its ubiquitous lack of relationship with other variables. The original lead level was used as the independent variable of interest (tested last in the model) with the five-year lead level serving as a concomitant variable. The two lead scores are highly correlated (Fig. 3), as are the original and follow-up IQ scores (Fig. 4). Interestingly, the simple correlation between follow-up lead and follow-up IQ (Fig. 5) is of the same magnitude as the correlation between original lead and follow-up IQ (Fig. 6). In the regression analysis, however, neither original lead nor follow-up lead (when concomitant variables are included in the regression model) predicted follow-up IQ ($F < 1$ in both cases). The only significant effect was for the concomitant variable term; $F(7,35) = 3.614$, $P < .01$. None of the individual predictors was significant. Apparently, the decline in lead levels, while

TABLE 2
CORRELATION MATRIX OF BLOOD LEAD LEVEL AND CHILD IQ (1977) AND CONCOMITANT VARIABLES

Variable	PbB	IQ	HOME	MatIQ	CA	Sex	SES	FaPr
Blood lead level (PbB)								
Child IQ	−0.276							
Caldwell HOME	−0.269	0.451						
Maternal IQ (MatIQ)	−.193	.379	.522					
Chronological age (CA)	−.068	−.254	.089	.029				
Sex	−.072	.130	.123	−.028	.062			
Socioeconomic status (SES)	.183	−.449	−.624	−.475	−.143	−.064		
Father present (FaPr)	−.010	.165	.433	.178	.161	.054	−.495	
Number of siblings (Sibs)	.314	−.284	−.202	−.177	.116	−.003	.161	−.064

not appreciably disturbing the structure of individual differences of lead on IQ, was sufficient to negate its relationship to IQ when confounding factors were controlled. Nor were these results due to sampling bias at follow-up. Table 3 shows that the demographic characteristics of those who returned for follow-up and those who did not were very similar. Maternal IQ was also stable from the 1978–1983 samples (83 vs 82) as was socioeconomic status (63.0 vs 64.8).

Another indirect test of an effect of lead on child IQ might be to examine its effect on the relationship between maternal and child IQ (Perino and Ernhart, 1974). According to the polygenetic model of hereditability intelligence (Bouchard and McGue, 1981), one would expect the correlation between maternal IQ and child IQ to be about 0.50. Lead might disrupt this relationship, as has been found by Bellinger and Needleman (1983). A similar result was found in the present studies. In the initial study, the correlation between maternal and child IQ for the

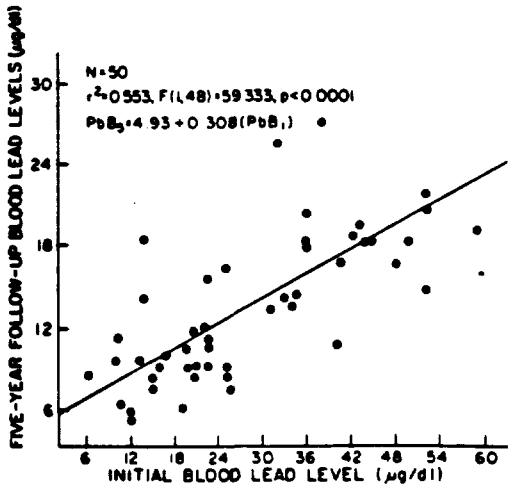

FIG. 3. Five-year follow-up blood lead levels (1983) as a function of initial blood lead levels (1977–1978) for 50 of the original subjects.

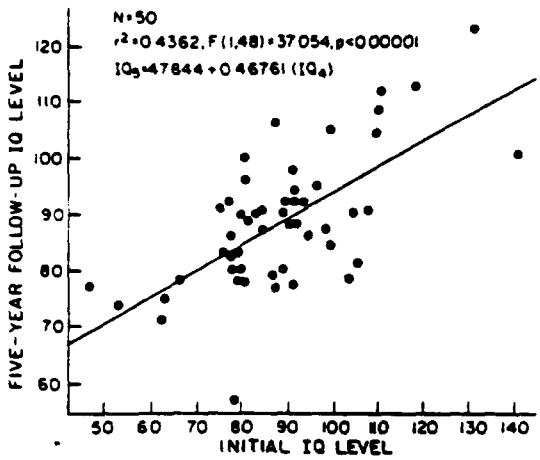

FIG. 4. Five-year follow-up IQ levels (1983) as a function of initial IQ levels (1977–1978).

children with blood lead levels of 6–30 μg/dl was 0.528; for children with blood lead levels of 31–56 μg/dl, it was 0.058. At five-year follow-up, when all blood lead levels were at or below 30 μg/dl, the correlation was back up to 0.45. From Fig. 7 it can be seen that about half of these children had had blood lead levels above 30 μg/dl and half below that level in 1977–1978.

SUMMARY

It appears that, in a high-risk population which had shown effects of lead on IQ, a reduction in lead levels resulted in a reduction of this effect 5 years later.

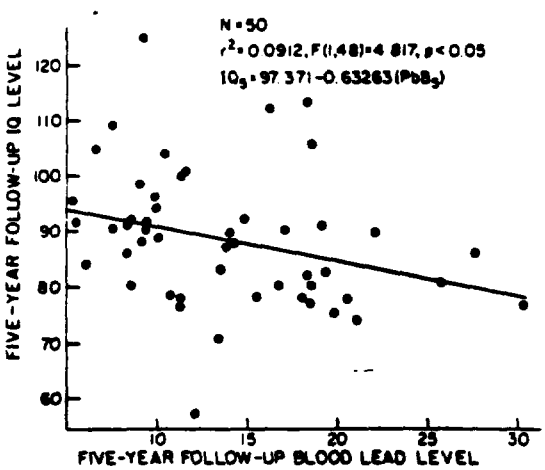

FIG. 5. Five-year follow-up IQ levels (1983) as a function of five-year follow-up blood lead levels (1983).

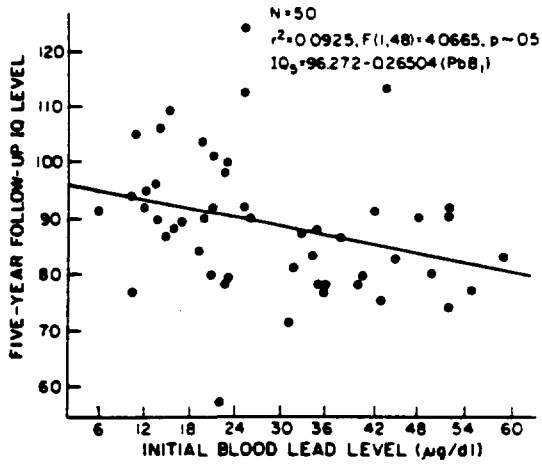

FIG. 6. Five-year follow-up IQ levels (1983) as a function of initial blood lead levels (1977–1978).

This disrupted relationship between maternal and child IQ returned to near the expected level once decreases in blood lead level occurred. Furthermore, it appeared that the effect of the major covariates was relatively homogeneous over time. Finally, controlling for SES appears to capture much of the variance related to other covariates due to multicolinearity—e.g., caregiver practices, maternal IQ, number of siblings, and exposure history. This would suggest that, for a given population, if one controlled for the major covariates—i.e., SES, caregiver environment, maternal IQ, age and exposure history—then other related covariates would be considerably less important in terms of the degree to which failure to control for them would distort the results.

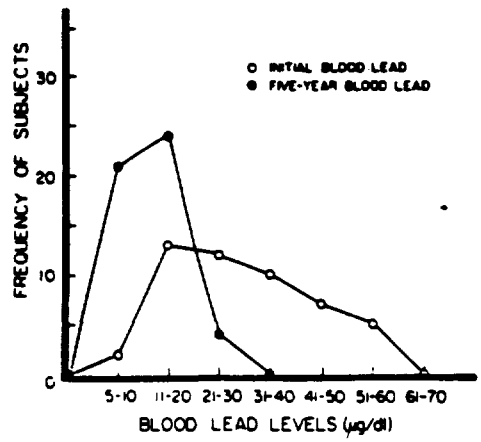

FIG. 7. Frequency distribution comparing initial and 5-year follow-up lead levels after lead abatement had occurred for 50 subjects.

TABLE 3
INITIAL (1978) SCORES OF CHILDREN ON KEY VARIABLES WHO WERE OR WERE NOT FOLLOWED UP 5 YEARS LATER

Key variable	Followed-up	
	Yes (SD)	No (SD)
Mean blood lead level	28.7 (14.0)	30.5 (11.6)
Mean child IQ	88.0 (17.3)	87.8 (16.7)
Mean Caldwell HOME	47.5 (20.6)	43.9 (26.1)
Mean maternal IQ	80.5 (9.8)	80.3 (10.1)
Mean chronological age (Months)	37.0 (18.0)	35.1 (23.2)
Mean socioeconomic class	4.6 (0.6)	4.5 (0.7)

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